Provider Playbook:
COVID-19 Outpatient Therapeutics

May 2022

NC DEPARTMENT OF HEALTH AND HUMAN SERVICES

PROVIDER PLAYBOOK: PREFACE

The policies outlined in this playbook should be regarded as guidance provided by the National Institute of Health (NIH), Food and Drug Administration (FDA), and the North Carolina Department of Health and Human Services (NC DHHS). This playbook does not cover every clinical scenario and providers should employ clinical decision making as allowed by their licensure scope of practice.

This playbook covers outpatient COVID-19 treatment options available in the state of North Carolina and associated provider guidance and responsibilities necessary to provide COVID-19 therapies.

TABLE OF CONTENTS (1 OF 2)

Please refer to this key throughout to find relevant information:
Monoclonal Antibodies Antivirals

TABLE OF CONTENTS (2 OF 2)

Please refer to this key throughout to find relevant information:
Monoclonal Antibodies Antivirals

All COVID-19 Treatment Options

PRODUCT SPECIFICATIONS (1 OF 2)

Bebtelovimab

- Manufactured by: Eli Lilly and Company
- Authorized dosage for bebtelovimab for treatment is 175 mg of bebtelovimab
- Bebtelovimab is authorized in adults and pediatric patients (12 years of age and older and weighing at least 40 kg)
- Bebtelovimab can only be delivered as a single intravenous injection over at least 30 seconds
- Bebtelovimab is authorized for treatment in patients with a positive COVID-19 test who are at high risk for progression to severe COVID-19, **and** for whom alternative COVID-19 treatment options approved or authorized by FDA are not accessible or clinically appropriate (FDA does not consider VEKLURY to be an adequate alternative to bebtelovimab for this authorized use because it may not be feasible or practical for certain patients)
- Providers should clinically monitor patients for at least one hour after infusion is complete for reactions
- Visit the Health Care Provider Fact Sheet for further provider guidance and information

EVUSHELD

- Manufactured: AstraZeneca
- Authorized dosage for EVUSHELD, formerly known as AZD7442, is a combination of two LAABs for pre-exposure prevention as 300 mg of tixagevimab and 300 mg of cilgavimab administered in two separate, consecutive injections
- EVUSHELD is authorized for adults and adolescents with moderate to severe immune compromise who may not mount an adequate immune response to COVID-19 vaccinations
- EVUSHELD can only be delivered as an intramuscular dose
- EVUSHELD is not yet approved for COVID-19 prophylaxis and treatment
- Patients who received only the previously authorized initial dose (150 mg of tixagevimab and 150 mg of cilgavimab) should receive an additional dose as soon as possible, with the dose based on the following criteria: 1) If the patient received their initial dose ≤ 3 months ago, the patient should receive a dose of 150 mg of tixagevimab and 150 mg of cilgavimab, and 2) If the patient received their initial dose > 3 months ago, the patient should receive a dose of 300 mg of tixagevimab and 300 mg of cilgavimab
- Providers should clinically monitor patients for at least one hour following the injection for reactions
- Timing for receiving additional doses of EVUSHELD, beyond the initial 600 mg, is still being studied
- Visit the Health Care Provider Fact Sheet for further provider guidance and information

PRODUCT SPECIFICATIONS (2 OF 2)

PAXLOVID

- Manufactured by: Pfizer
- Authorized standard dosage for PAXLOVID is a combination of 300 mg nirmatrelvir (two 150 mg tablets) with 100 mg ritonavir (one 100 mg tablet), taken together orally twice daily for 5 days, with or without food
- Authorized renal impairment dosage for patients with moderate renal impairment (eGFR ≥30 to <60 mL/min) is 150 mg nirmatrelvir (one 150 mg tablet) with 100 mg ritonavir (one 100 mg tablet), taken together orally twice daily for 5 days, with or without food
- PAXLOVID is authorized for adults and pediatric patients (age 12 and older)
- PAXLOVID can only be delivered as an oral pill
- PAXLOVID is authorized for treatment in patients with a positive COVID-19 test who are at high risk for progression to severe COVID-19
- Providers should monitor patients with potential drug interactions (list available here) for adverse reactions
- Visit the Health Care Provider Fact Sheet for further provider guidance and information

LAGEVRIO (molnupiravir)

- Manufactured by: Merck
- Authorized dosage for molnupiravir is 800 mg (four 200 mg capsules) taken orally every 12 hours for 5 days, with or without food
- Molnupiravir is only authorized for adults
- Molnupiravir can only be delivered as an oral pill
- Molnupiravir is authorized for treatment in patients with a positive COVID-19 test who are at high risk for progression to severe COVID-19, and for whom alternative COVID-19 treatment options are not accessible or clinically appropriate
- Providers should monitor patients with potential drug interactions for adverse reactions
- Visit the Health Care Provider Fact Sheet for further provider guidance and information

VEKLURY (remdesivir)

- Manufactured: Gilead Sciences, Inc.
- Approved dosage for VEKLURY varies, please refer to the dosage guidance here
- VEKLURY is a drug approved for the treatment of coronavirus disease 2019 (COVID-19) in adults and pediatric patients (28 days of age and older and weighing at least 3 kg) with positive results of direct severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) viral testing, who are: Hospitalized, or Not hospitalized and have mild-to-moderate COVID-19 and are at high risk for progression to severe COVID-19, including hospitalization or death
- VEKLURY can only be delivered as an intravenous (IV) infusion
- Providers should clinically monitor patients for at least one hour following the infusion for reactions
- Visit the Package Insert for further provider guidance and information

mAbs Treatment

MONOCLONAL ANTIBODIES – OVERVIEW

Monoclonal antibodies, or mAbs, are antibodies made in a laboratory to fight a particular infection. The Food and Drug Administration (FDA) has issued **Emergency Use Authorization (EUA)** for the use of monoclonal antibody therapies for adult and pediatric patients aged 12 and older. mAbs are given to patients with an infusion, subcutaneous injection, or intramuscular injection. They are used for treatment or prevention. The following mAb products are currently authorized and are effective against currently circulating SARS-CoV-2 variants:

Generic Name	Also known as	Authorized Indication	Route of Administration	Dosing Regimen	Authorized Patient Population	Standing Order?*	Efficacy
Bebtelovimab	**Bebtelovimab**	COVID-19 Treatment **within seven (7) days** of symptoms	Intravenous Infusion	175 mg of bebtelovimab	Patients aged **12 years and older** and weighing at least 40 kg	Yes, as of February 15th	Placebo controlled trial data not available to determine % effectiveness at reducing hospitalization Retains efficacy against Omicron and the BA.2 Omicron subvariant
Tixagevimab / cilgavimab	**EVUSHELD AZD7442**	Pre-exposure prophylaxis (PrEP)	Intramuscular Injection	300 mg of tixagevimab and 300 mg of cilgavimab	Patients aged **12 years and older** who are immunocompromised or have a contraindication for COVID-19 vaccines	No – per FDA/HHS	**77% effective** in preventing SARS-CoV-2 RT-PCR symptomatic illness Higher dose may be more likely to prevent infection by the COVID-19 Omicron subvariants BA.1 and BA.1.1

**Per the Public Readiness and Emergency Preparedness Act, pharmacies were added to the eligible providers and can now administer monoclonal antibody treatment*

Antiviral Treatments

ORAL ANTIVIRALS - OVERVIEW

The FDA has issued **EUAs** for the use of oral antiviral therapies for adult and pediatric patients aged 12 and older (molnupiravir authorized for 18+ only). Oral antivirals are administered orally and only used for treatment. The following oral antivirals products are currently authorized and are effective against currently circulating SARS-CoV-2 variants. Both therapeutics target mild-to-moderate COVID-19 for adults who are at risk of severe illness:

Generic Name	Also known as	Authorized Indication	Route of Administration	Administration Requirements	Dosing Regimen	Authorized Patient Population	Standing Order?	Efficacy
Molnupiravir	**MK-4482, Merck, LAGEVRIO**	Treatment of mild-to-moderate COVID-19 in adults who are at risk for progressing to severe COVID-19 and for whom alternate treatment is not accessible or clinically appropriate	Oral	Must start **within five (5) days** of symptom onset Not recommended during pregnancy	800 mg twice-daily for five (5) days	Adult patients **aged 18 years and older**	No – per FDA/HHS	**30% effective** in preventing hospitalizations or deaths within five (5) days of symptom onset Retains efficacy against Omicron
Nirmatrelvir / Ritonavir	**PAXLOVID, Pfizer**	Treatment of mild-to-moderate COVID-19 in adult and pediatric patients (12+) who are at risk for progressing to severe COVID-19	Oral	Must start **within five (5) days** of symptom onset Dosage adjustment required for moderate renal impairment (eGFR ≥30 to <60 mL/min) Extensive drug interactions list	**Standard:** 300 mg of nirmatrelvir and 100 mg of ritonavir twice-daily for five (5) days **Renal impairment:** 150 mg of nirmatrelvir and 100 mg of ritonavir twice-daily for five (5) days	Patients **aged 12 years and older**	No – per FDA/HHS	**88% effective** in preventing hospitalizations or deaths within five (5) days of symptom onset Expected to maintain effectiveness across all variants

VEKLURY (REMDESIVIR)- OVERVIEW

Please Note: VEKLURY (remdesivir) is not allocated by the federal government and only available commercially.

Veklury is an antiviral medication that works by inhibiting an enzyme that is essential for SARS-CoV-2 viral replication. The FDA has granted **full approval** for treatment in both hospitalized and non-hospitalized patients who are 12 years of age or older. The FDA has also granted **full approval** for treatment in both hospitalized and non-hospitalized patients at least 28 days of age and older and weighing at least 3 kg.

Please view full prescribing information here, https://www.gilead.com/-/media/files/pdfs/medicines/covid-19/veklury/veklury_pi.pdf and NIH Guidance here.

Generic Name	Also known as	Approved Indication	Route of Administration	Administration Requirements	Dosing Regimen	Approved Patient Population	Standing Order?	Efficacy
Remdesivir	**VEKLURY**	Treatment of COVID-19 for adult and pediatric patients who are hospitalized or not hospitalized and have mild to moderate COVID-19 and are at high risk for progression to severe COVID-19	Intravenous Infusion	May only be administered in settings in which healthcare providers have immediate access to medications to treat severe infusion or hypersensitivity reactions and the ability to activate EMS For non-hospitalized patients, treatment must be initiated as soon as possible after diagnosis and **within seven (7) days of symptom onset**	**For patients weighing 40kg or greater:** 200mg loading dose on Day 1, followed by a once-daily maintenance dose of 100mg from Day 2 **For patients weighing less than 40kg:** 5mg/kg loading dose on Day 1, followed by a once-daily maintenance dose of 2.5mg/kg from Day 2 **Treatment duration**: Hospitalized patients - 5-10 days total, Non-hospitalized patients – three (3) days total	Adults and pediatric patients **28 days of age and older and weighing at least 3 kg**	No	**87% effective** at preventing hospitalization/death compared to placebo in non-hospitalized patients considered at high-risk for progression to severe COVID-19 Retains efficacy against Omicron

Treatment Prioritization

PRIORITIZATION OF COVID-19 THERAPEUTICS

COVID-19 therapy is open to all individuals who qualify, per the terms of the EUAs and FDA guidance

Currently, COVID-19 therapies, especially oral antivirals, are widely available across the state. Anyone with a COVID-19 diagnosis who is considered high risk should be carefully evaluated for potential treatment options, and treatment should not be withheld if the patient qualifies under the EUA.

During surges in cases of SARS-CoV-2 infection, logistical or supply constraints may make it impossible to offer available therapeutics to all the non-hospitalized patients who are eligible to receive them. In these situations, it may be necessary to prioritize therapy based on age, vaccination status, immune status, or presence of risk factors.

NCDHHS is continuously monitoring supply of all COVID-19 therapeutics and will update these recommendations on patient prioritization, as necessary.

ALL TREATMENT PRODUCTS PRIORITIZATION

Treatment Products

For non-hospitalized patients with mild to moderate COVID-19 who are at high risk of disease progression, the NIH Panel recommends using one (1) of the following therapeutics (listed in order of preference):

1. PAXLOVID
2. Remdesivir*

If none of the preferred therapies for high-risk, non-hospitalized patients are available, feasible to deliver, or clinically appropriate (e.g., due to drug-drug interactions, concerns related to renal or hepatic function), the Panel recommends using 1 of the following therapies (listed in alphabetical order):

1. Bebtelovimab
2. Molnupiravir

Note: At this time, REGEN-COV and bamlanivimab and etesevimab are no longer authorized for use due to available data that shows these products are not effective against the Omicron variant. Sotrovimab is no longer authorized for use due to available data that shows it is not effective against the BA.2 Omicron sub-variant.

**Remdesivir is not allocated by the federal government and is only available for private purchase*

HEALTH ALERT NETWORK HEALTH ADVISORY AND NC PROVIDER MEMO

A large proportion of the North Carolina population is considered high risk based on age or underlying conditions. Therefore, anyone with a COVID-19 diagnosis should be carefully evaluated for potential treatment options. These therapies have demonstrated effectiveness against currently circulating SARS- CoV-2 variants, and many have been clinically proven to be effective in preventing hospitalization or death.

Please refer to this memo for provider guidance for outpatient treatment and prevention of coronavirus disease 2019 (COVID-19) in patients who are at high risk of progressing to severe disease.

Health Alert Network (HAN) Health Advisory (linked):

The Centers for Disease Control and Prevention (CDC) has issued this Health Alert Network (HAN) Health Advisory to update healthcare providers, public health departments, and the public about the availability and use of recommended therapies for COVID-19 and to advise against using unproven treatments that have known or potential harms for outpatients with mild to moderate COVID-19. For patients with mild to moderate COVID-19 who are not hospitalized and who are at increased risk for severe COVID-19 outcomes, several treatment options, including antiviral medications and monoclonal antibodies, are now widely available and accessible.

COVID-19 OUTPATIENT THERAPEUTICS DECISION GUIDE

COVID-19 Outpatient Therapeutics

Clinical Decision Aid for Ages 12+

Adult or pediatric patient (ages 12 and older weighing at least 40 kg) with mild to moderate COVID-19 and at high risk for progression to severe disease

Is patient:

- Hospitalized for COVID-19

OR

- Requiring O_2

OR

- Requiring an increase in baseline home O_2 due to COVID-19?

NO → Symptom onset within the past 5–7 days?

YES → Consider one of the following therapeutics, if available, feasible, and clinically appropriate[1]:

Paxlovid[2] within 5 days of symptom onset If patient does not have severe renal impairment (eGFR <30mL/min OR severe hepatic impairment (Child-Pugh Class C)

- **eGFR ≥ 60 mL/min:** 300 mg nirmatrelvir taken with 100 mg ritonavir twice daily for 5 days
- **eGFR ≥ 30 to < 60:** 150 mg nirmatrelvir taken together with 100 mg ritonavir twice daily for 5 days
- Evaluate concomitant use of CYP3A inducers and medications with high dependency on CYP3A for clearance as these may be contraindicated[2,3]

OR

Veklury (remdesivir)[4] 200 mg IV x 1 dose on Day 1, 100 mg IV x 1 on Days 2–3 begun **ASAP within 7 days of symptom onset**

NO → Symptom onset within the past 5–7 days?

YES → **If Paxlovid and Veklury (remdesivir) are not available, feasible or clinically appropriate consider one of the following therapeutics:**

bebtelovimab[5] ASAP within 7 days of symptom onset
175 mg single IV injection

OR

Lagevrio (molnupiravir)[6] If patient age 18 or older AND possibility of pregnancy, if applicable, ruled out:

800 mg by mouth every 12h for 5 days begun
ASAP within 5 days of symptom onset

Prescribers must review and comply with the mandatory requirements outlined in the **Lagevrio (molnupiravir) EUA[6]**

Treatment of symptoms, management per NIH & CDC Guidelines

References:

1 NIH's COVID-19 Treatment Guidelines Therapeutic Management of Nonhospitalized Adults With COVID-19. https://www.covid19treatmentguidelines.nih.gov/therapies/statement-on-therapies-for-high-risk-nonhospitalized-patients/
2 Paxlovid EUA. https://www.fda.gov/media/155050/download
3 NIH's COVID-19 Treatment Guidelines Panel: Ritonavir-Boosted Nirmatrelvir (Paxlovid). https://www.covid19treatmentguidelines.nih.gov/therapies/antiviral-therapy/ritonavir-boosted-nirmatrelvir--paxlovid-/
4 Veklury (remdesivir) Prescribing Information. https://www.gilead.com/-/media/files/pdfs/medicines/covid-19/veklury/veklury_pi.pdf
5 Bebtelovimab EUA. https://www.fda.gov/media/156152/download
6 Lagevrio EUA. https://www.fda.gov/media/155054/download

ASPR ASSISTANT SECRETARY FOR PREPAREDNESS AND RESPONSE

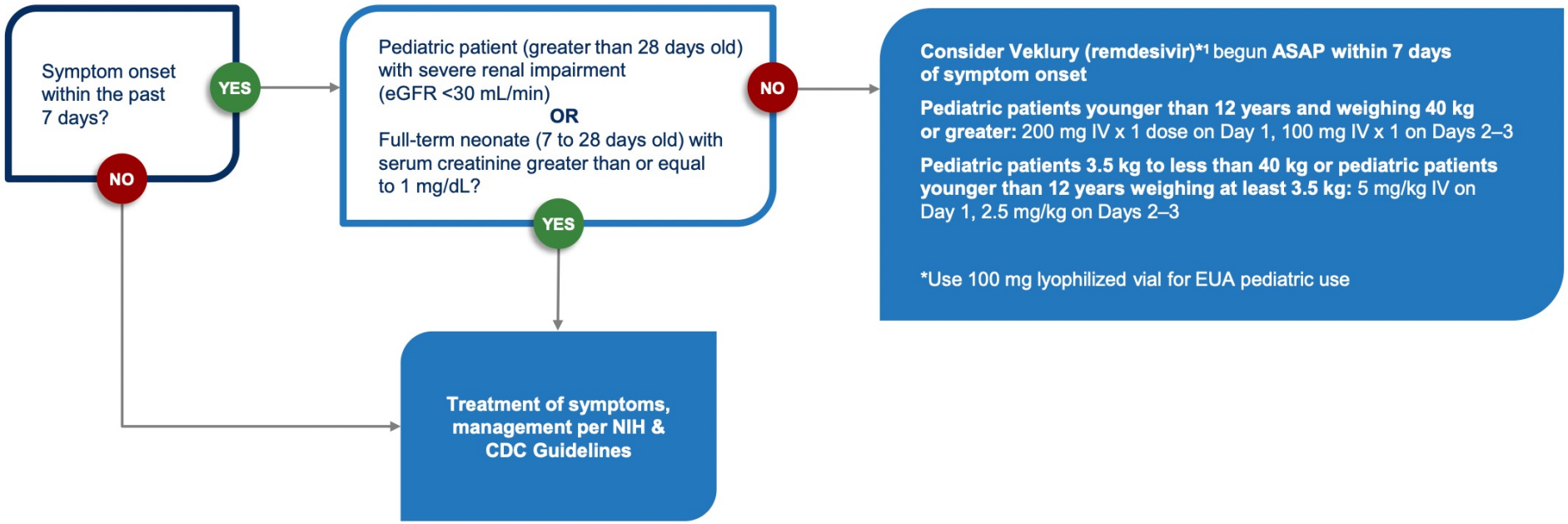
April 18, 2022

COVID-19 OUTPATIENT THERAPEUTICS DECISION GUIDE – PEDIATRIC PATIENTS

Clinical Decision Aid for Pediatric Patients

Outpatient **3.5 kg to less than 40 kg** or **younger than 12 years of age weighing at least 3.5 kg**, with mild to moderate COVID-19 and at high risk for progression to severe disease

Update as of April 25th: Patients must be 28 days of age or older and weigh at least 7 pounds (3 kg) in order to receive Veklury



Reference:

[1] Veklury (remdesivir) EUA: https://www.fda.gov/media/137566/download.

ASPR ASSISTANT SECRETARY FOR PREPAREDNESS AND RESPONSE

April 18, 2022

NC DEPARTMENT OF HEALTH AND HUMAN SERVICES

Registration

NEW PROVIDER REGISTRATION

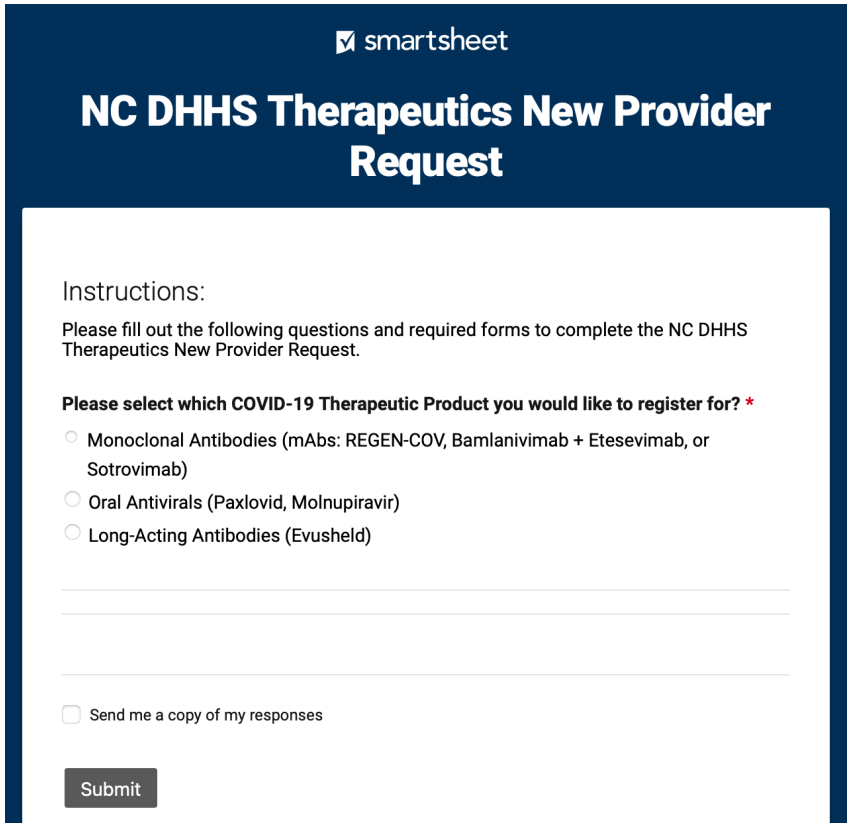
New providers should register with the state's COVID-19 treatment program for all COVID-19 therapeutic products by completing **NC DHHS Therapeutics New Provider Request Form**. NC DHHS will then create your account in the Health Partners Ordering Portal (HPOP) as a registered provider.*

Registration Requirements:

- When your account is created in HPOP, you will receive an email from vpop_no_reply@cdc.gov allowing you complete the enrollment process
- To activate your account, you must verify your site address and receiving hours. You must complete these steps to request allocations

It will take 2-3 business days to process your registration. Registration does not guarantee that you will receive allocation.

For additional guidance please visit the HPOP Provider Portal - Get Started.



Ordering therapeutics and provider registration has transitioned from the C19 ABC Portal to HPOP as of 14 FEB 22.

TEST TO TREAT (T2T) OVERVIEW

Test to Treat (T2T) is a nationwide initiative that provides individuals a more effective way to rapidly access lifesaving treatment for COVID-19

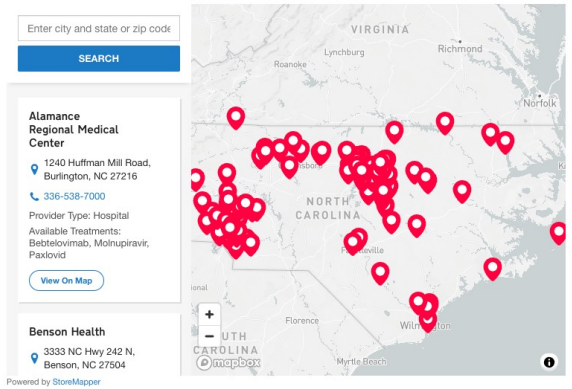
In this program, people can get tested and – if they are positive and treatments are appropriate for them – receive a prescription from a healthcare provider, and have their prescription filled all in one location.

If interested in becoming a Test to Treat provider, please fill out the Test to Treat Program Eligibility Survey. Please see requirements below:

- Rapid COVID-19 testing on-site (or evaluation of at-home testing)
- Linkage to a clinical evaluation by licensed healthcare provider after positive result to provide prescription when appropriate
- Co-located pharmacy* able to readily dispense medication to eligible patients
- Provide services to all individuals, regardless of insurance status

Click here to view the COVID-19 Test to Treat Fact Sheet

Providers who meet these criteria have the option to be identified as a Test to Treat location on both the NC DHHS and the federal COVID-19 Therapeutics Site Finder Tool



Providers must maintain ADA compliance. Contact the provider for information about access for people with disabilities.

Note: The Test to Treat Site Finder, found here, is available and accessible for the general public seeking COVID-19 treatment

*See next slide for NC specific dispensing guidance

ORAL ANTIVIRAL DISPENSING GUIDANCE

Physicians, advanced practice registered nurses, and physician's assistants with active licensure and in good standing with their respective governing bodies can prescribe and dispense oral antivirals for treatment of COVID-19 in accordance with the PAXLOVID and molnupiravir EUAs, from their offices, if the following conditions are met:

1. There is absolutely no charge to the patient for the drug or act of dispensing, including seeking reimbursement of dispensing fees through third-party payors
2. Products are labeled in accordance with State and Federal dispensing laws. Details from the NC Board of Pharmacy on what information must be included on a prescription label can be found here

Physicians who wish to dispense oral antivirals for the treatment of COVID-19 (or any other medication) for a fee must be registered with the NC Board of Pharmacy as a dispensing physician.

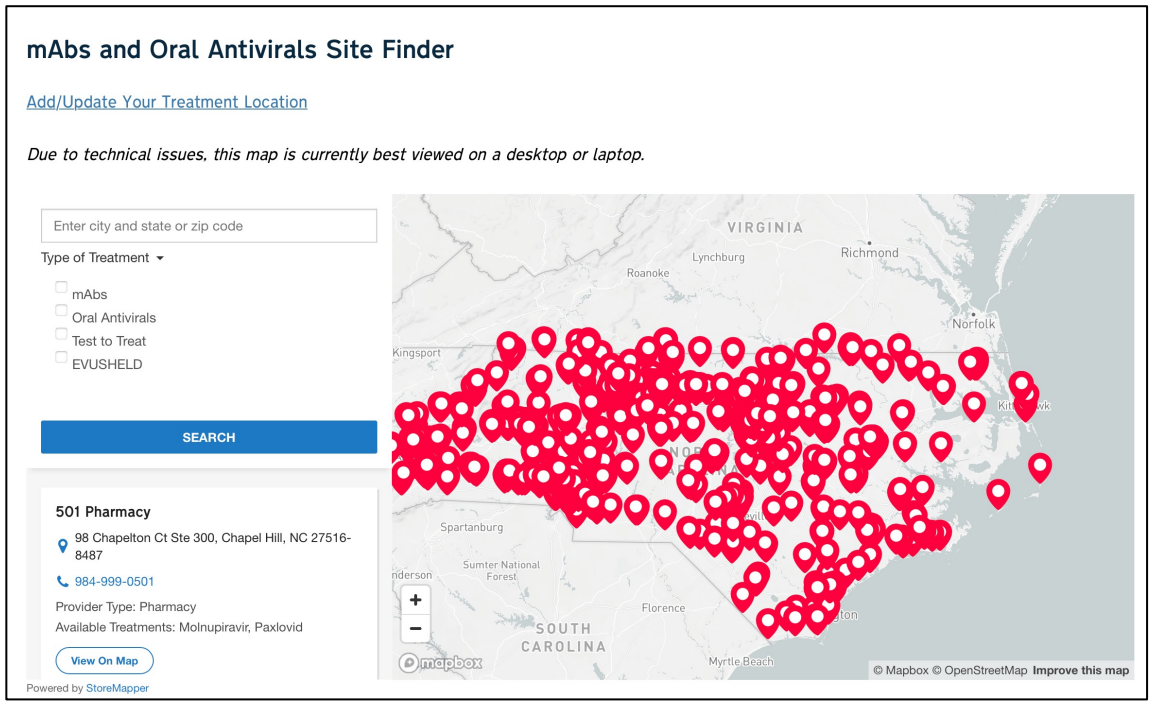
Nurse Practitioners and Physician's Assistants who wish to dispense medications other than COVID-19 therapeutics (whether a fee is charged or not) or who wish to dispense COVID-19 therapeutics for a fee must register with the Board of Pharmacy as a nurse practitioner or physician's assistant.

For more information on becoming a dispensing physician, nurse practitioner, or physician's assistant please visit the NC Board of Pharmacy Dispensing Physician, Physician Assistant and Nurse Practitioners Registration Requirements.

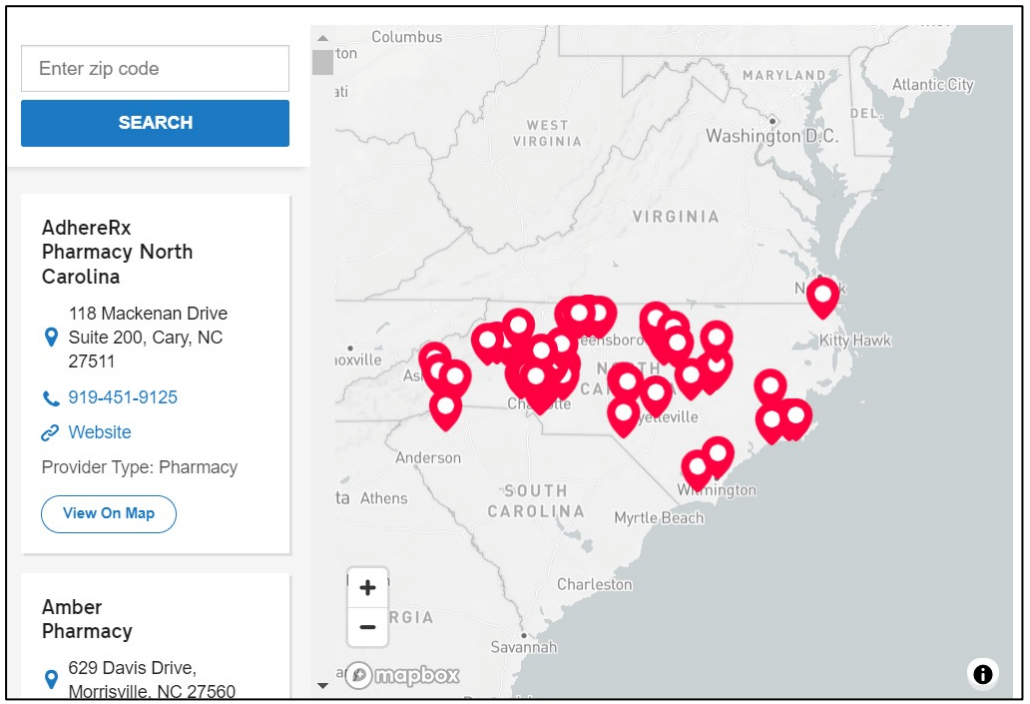
Allocation & Site Finder

HOW TO LOCATE COVID-19 THERAPEUTICS

mAbs and Oral Antivirals Site Finder Tool



EVUSHELD Site Finder Tool



The ‘Find COVID-19 Treatment’ section on the NC DHHS website includes an updated ‘Site Finder’ tool that enables recipients to: 1) Search for nearby treatment sites, 2) Discover available treatments each site offers for administration, 3) Find resources to schedule an appointment (phone numbers, websites)

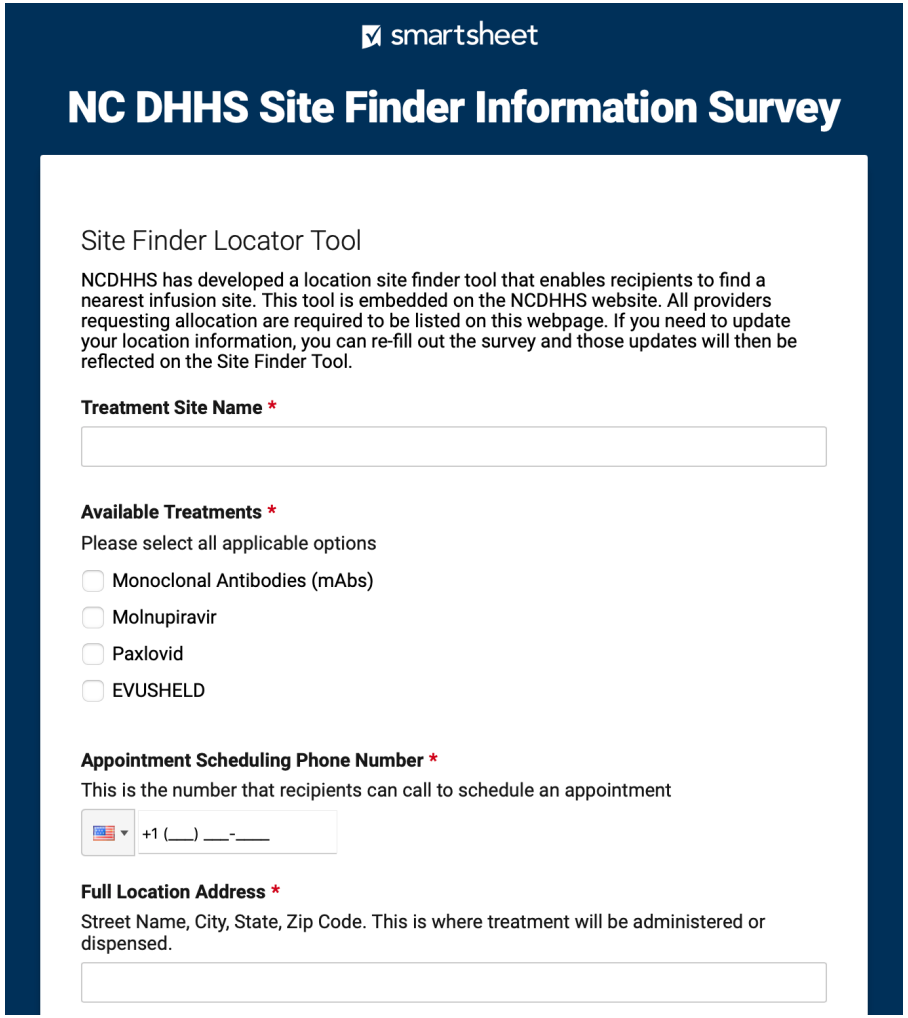
The ‘Information For Individuals at Higher Risk’ section on the NC DHHS website includes a ‘Site Finder’ tool specifically for EVUSHELD treatment locations

SITE FINDER REGISTRATION

All providers serving the greater population (excluding long-term care facilities, hub locations, and non-public facing providers) requesting mAbs or oral antivirals allocations are **required** to be listed on the NC DHHS website so that community members seeking treatment are aware that your facility may be able to serve them. **All providers will be automatically added to the Site Finder upon receiving allocation or reporting administrations.**

To update, delete, or add missing information to your posting on the Site Finder tool, please complete the Site Finder Provider Information survey.

Your location will be listed on the mAbs and Oral Antivirals Site Finder Tool and/or the EVUSHELD Site Finder Tool embedded on the NC DHHS website. This ensures all eligible recipients can easily and equitably locate, access, and schedule appointments to receive this potentially lifesaving treatment.



UPDATED THERAPEUTICS ALLOCATION RESTRICTIONS

Allocation requests will be denied or reduced if provider locations have more than three (3) weeks of on-hand inventory of the requested product

If you are denied allocation and have an urgent need for additional product:

- Please first check the NC COVID-19 Therapeutics Transfer Marketplace
  - If you are unable to find a transfer partner, then please reach out to therapeutics.COVID19@dhhs.nc.gov
- Once your on-hand inventory is less than your 3-week utilization history, please feel free to re-request additional product via the appropriate request form found in the Provider Hub

Inventory and Administration Tracking Message for Providers

If your current inventory of any product and your 3-week administration total differs from the numbers you have self-reported of administrations and inventory to HPOP & the NC Admin/Inventory Report, providers should notify therapeutics.COVID19@dhhs.nc.gov with the correct numbers so that we may have an accurate reporting to properly assess requests and ensure that product is allocated where it is most needed.

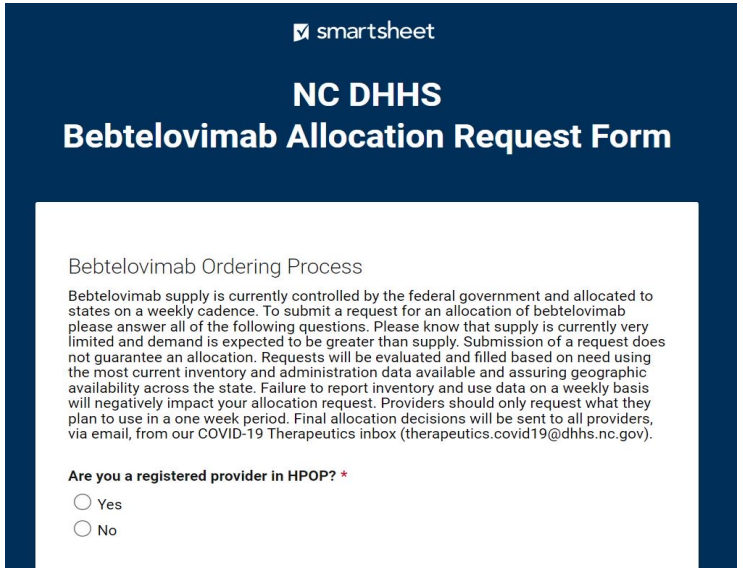
REQUESTING MABS ALLOCATIONS (1 OF 3)

NC DHHS is responsible for the **management and distribution of mAbs treatment allocations** requested by providers within the state.

To request product: Complete the Bebtelovimab Allocation Request Survey.

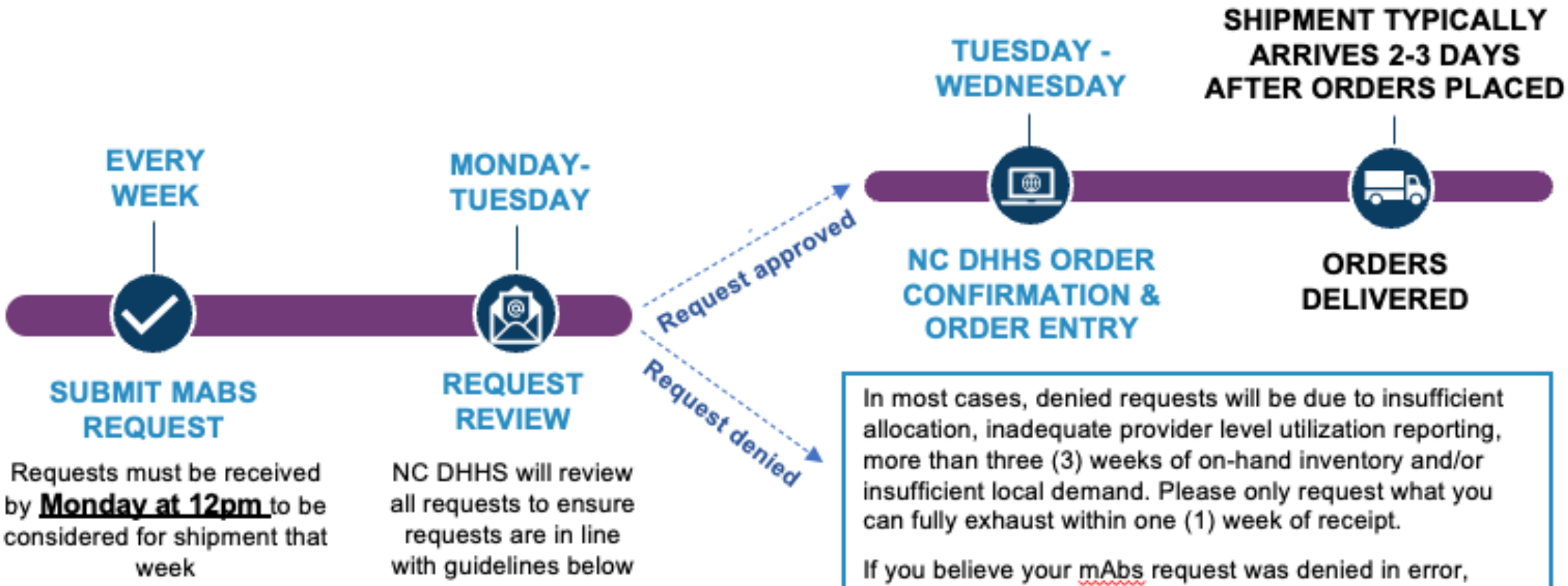
- Providers must be registered in HPOP to request monoclonal antibodies
- Providers must submit allocation requests by **Mondays, every week at 12pm EST,** to be eligible to receive mAbs shipments. Requests will be processed on Monday afternoons
- There is not an option to return product to the manufacturer. Please only request the number of courses you can **administer within seven (7) days and** hold no more than **three (3) weeks of on-hand inventory**. If extra product is available on-hand, please facilitate a transfer with another facility in need of that product
- Providers should always submit allocation requests in number of courses

NC DHHS will send order confirmations of allocation request receipts via the Therapeutics Mailbox every Wednesday.



Bebtelovimab Requests

REQUESTING MABS ALLOCATIONS (2 OF 3)



To request and receive shipment, providers must be registered with HPOP. For the current registration process, please refer to slide 18.

REQUESTING MABS ALLOCATIONS (3 OF 3)

NC DHHS reviews all requests to ensure orders align with state ordering guidelines and meet a specific set of criteria.

This criteria is determined by HHS on the number of weekly allocation amounts provided to the state and on the number of requests received by the state from the Allocation Request Forms submitted by providers. State ordering guidelines for mAbs is provided below:

	Bebtelovimab (Eli Lilly)
Minimum Order Quantity (MOQ)	**10**
Maximum Order Request	If requesting > MOQ: Only order enough inventory to meet **one (1) week of utilization demand**
Reporting Method	**All administrations must be reported daily via the HPOP when location is open**
Direct Ship Available	✓

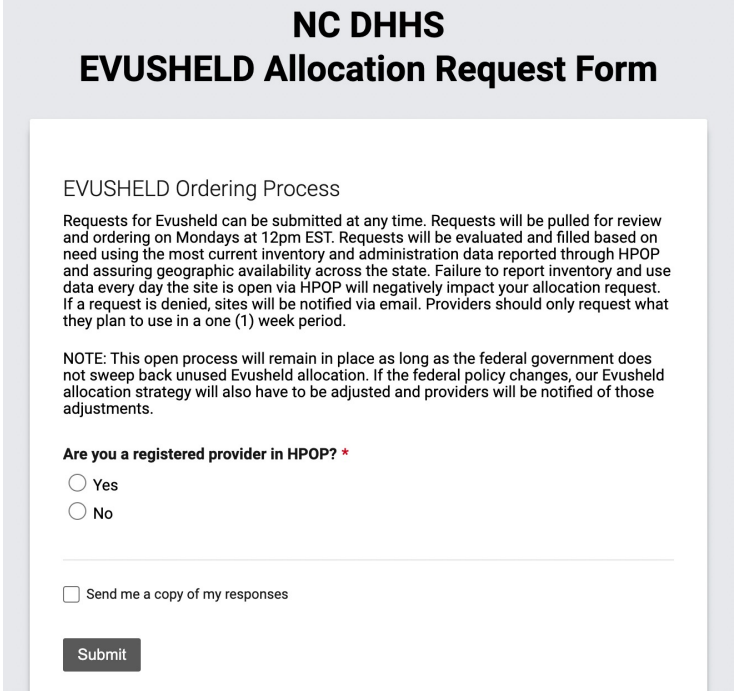
REQUESTING EVUSHELD ALLOCATION (1 OF 3)

NC DHHS is responsible for the **management and distribution of EVUSHELD allocations** requested by providers within the state.

To Request product: Complete the EVUSHELD Allocation Request Form.

- **Providers can submit allocation requests at any time**. Requests will be processed on **Mondays, every week at 12pm EST**
- There is not an option to return product to the manufacturer. Please only request the number of courses you can **administer within seven (7) days and** hold no more than **three (3) weeks of on-hand inventory**. If extra product is available on-hand, please facilitate a transfer with another facility in need of that product
- Providers should always submit allocation requests in number of **cartons.** As a reminder, the updated initial dose for EVUSHELD requires two cartons of product per patient. A "catch-up" dose of EVUSHELD requires one carton of product

Confirmation of allocation request receipt is distributed from the Therapeutics Mailbox every Tuesday.



NC DHHS
EVUSHELD Allocation Request Form

EVUSHELD Ordering Process

Requests for Evusheld can be submitted at any time. Requests will be pulled for review and ordering on Mondays at 12pm EST. Requests will be evaluated and filled based on need using the most current inventory and administration data reported through HPOP and assuring geographic availability across the state. Failure to report inventory and use data every day the site is open via HPOP will negatively impact your allocation request. If a request is denied, sites will be notified via email. Providers should only request what they plan to use in a one (1) week period.

NOTE: This open process will remain in place as long as the federal government does not sweep back unused Evusheld allocation. If the federal policy changes, our Evusheld allocation strategy will also have to be adjusted and providers will be notified of those adjustments.

Are you a registered provider in HPOP? *

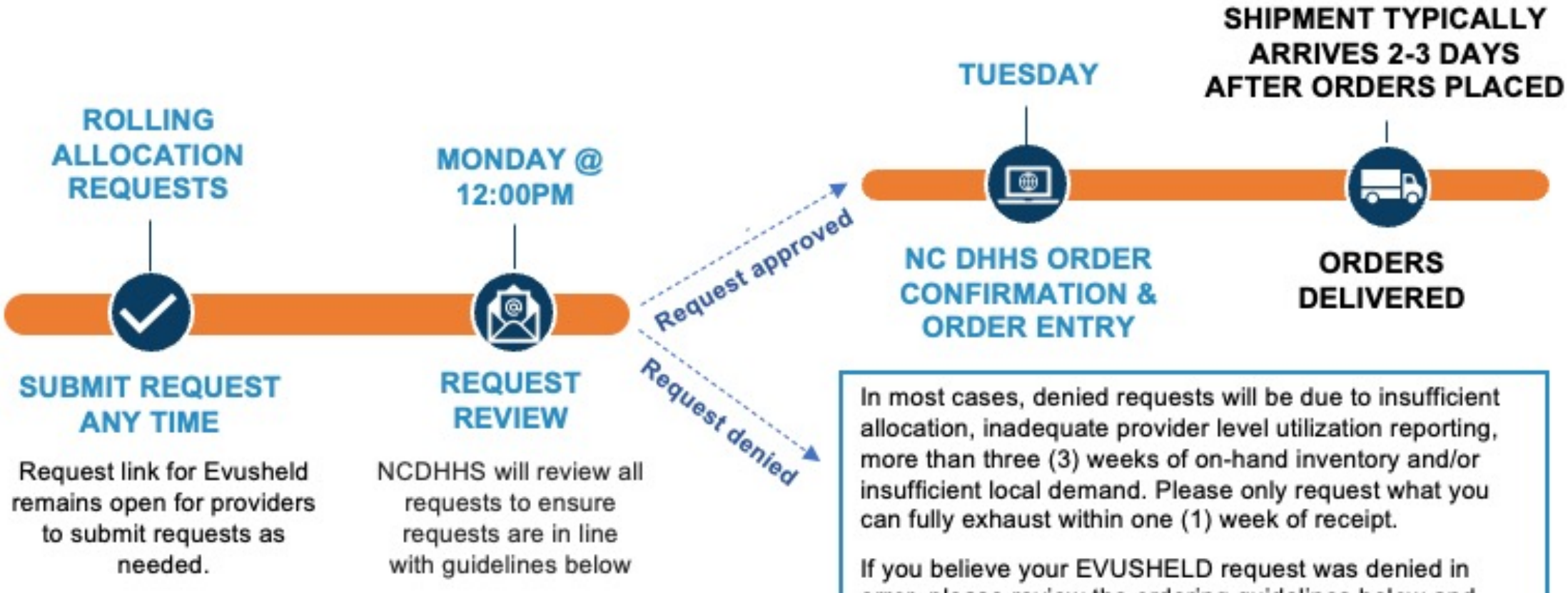
- ○ Yes
- ○ No

☐ Send me a copy of my responses

Submit

EVUSHELD Requests

REQUESTING EVUSHELD ALLOCATIONS (2 OF 3)



To request and receive shipment, providers must be registered within HPOP. For the current registration process, please refer to slide 19.

REQUESTING EVUSHELD ALLOCATIONS (3 OF 3)

NC DHHS reviews all requests to ensure orders align with state ordering guidelines and meet a specific set of criteria.

This criteria is determined by the HHS on the number of weekly allocation amounts provided to the state and on the number of requests received by the state from the Allocation Request Forms submitted by providers. State ordering guidelines for EVUSHELD is provided below:

	EVUSHELD (AstraZeneca)
Minimum Order Quantity (MOQ)	**24**
Maximum Order Request	If requesting > MOQ: Only order enough inventory to meet **one (1) week of utilization demand**
Reporting Method	**All administrations must be reported DAILY in cartons via the Health Partner Ordering Portal (HPOP)**
Direct Ship Available	✓

REQUESTING ORAL ANTIVIRALS ALLOCATION (1 OF 3)

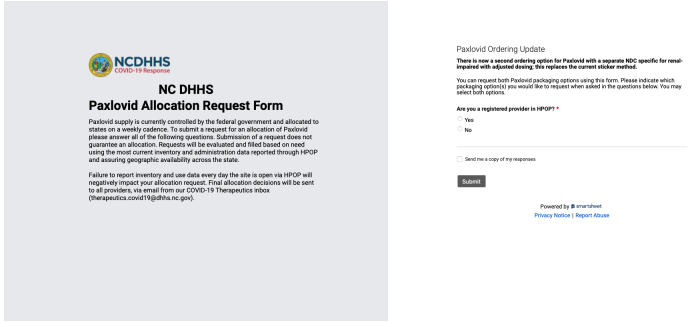
NC DHHS is responsible for the **management and distribution of oral antivirals treatment allocations** requested by providers within the state.

To request product: Complete the PAXLOVID Allocation Request Survey and/or the Molnupiravir Allocation Request Survey.

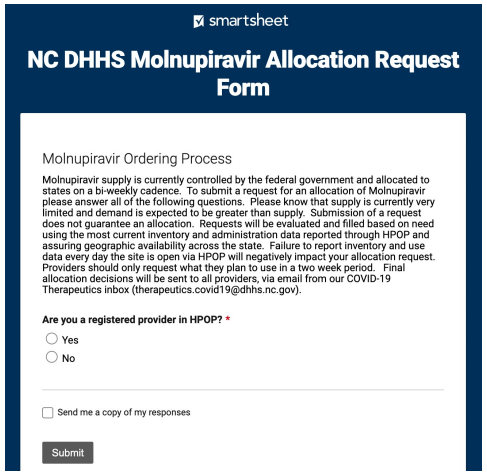
- Providers must be registered in HPOP to request oral antivirals
- Providers must submit oral antiviral allocation requests by **Mondays, every week at 12pm EST** to be eligible to receive shipment
- There is not an option to return product to the manufacturer. Please only request the number of courses you can **administer within seven (7) days** and hold no more than **three (3) weeks of on-hand inventory**. If extra product is available on-hand, please facilitate a transfer with another facility in need of that product
- Providers should always submit allocation requests in number of courses

Confirmation of allocation request receipt is distributed from the Therapeutics Mailbox every Wednesday.

"Renal" PAXLOVID Note: As of April 14th, 2022, Pfizer offers a "renal" PAXLOVID packaging. This packaging contains the 150mg nirmatrelvir with 100 mg ritonavir dosing required for renally impaired patients and replaces the sticker method providers have previously used to manually adjust regular PAXLOVID packaging. "Renal" PAXLOVID can be requested using the existing PAXLOVID request survey.

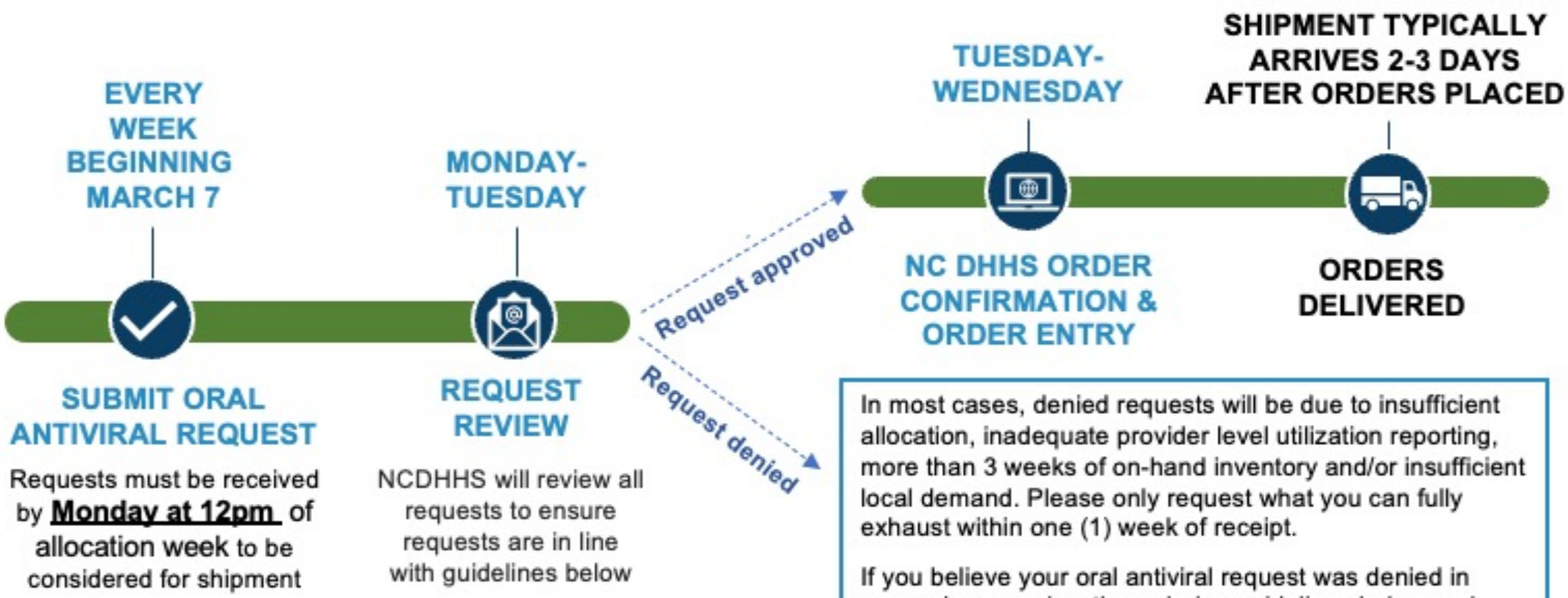


PAXLOVID Requests



Molnupiravir Requests

REQUESTING ORAL ANTIVIRALS ALLOCATIONS (2 OF 3)



To request and receive shipment, providers must be registered within the HPOP. For the current registration process, please refer to slide 19.

REQUESTING ORAL ANTIVIRALS ALLOCATIONS (3 OF 3)

NC DHHS reviews all requests to ensure orders align with state ordering guidelines and meet a specific set of criteria.

This criteria is determined by the HHS on the number of weekly allocation amounts provided to the state and on the number of requests received by the state from the Allocation Request Forms submitted by providers. State ordering guidelines for oral antivirals is provided below:

	Molnupiravir (Merck)	PAXLOVID – Standard Dosage (Pfizer)	PAXLOVID – Renal Dosage (Pfizer)
Minimum Order Quantity (MOQ)	**24**	**20**	**5**
Maximum Order Request	If requesting > MOQ: Only order enough inventory to meet **one (1) week of utilization demand**		
Reporting Method	**All administrations must be reported via the Health Partner Ordering Portal (HPOP) DAILY when location is open**		
Direct Ship Available	✓	✓	✓

NC DEPARTMENT OF HEALTH AND HUMAN SERVICES

Shipping & Storage

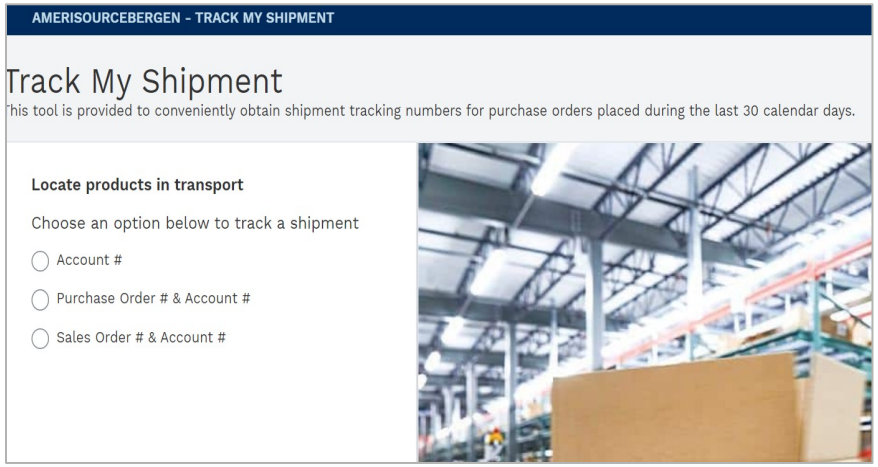
SHIPPING & STORAGE

Shipping:

ABC **fulfills and ships mAb and oral antiviral product orders**. NC DHHS does not control these functions.

Visit ABC's Tracking Tool Website to track order status.

- Use account # provided by ABC
- ABC delivers the drug to the site of care
- The product is shipped refrigerated and must be stored refrigerated
- If request is approved, NC DHHS confirms and enters orders by Friday of the same week. Expected delivery time of orders is the following Tuesday at the latest
- For access and more information regarding ABC shipping, contact customersystemsupport@AmerisourceBergen.com



Storage:

- **mAbs:** Provider must store product refrigerated at 2° C to 8° C (36° F to 46° F) in the original carton to protect from light before use. Discard any unused portion. DO NOT FREEZE. DO NOT SHAKE
- **Oral Antivirals:** Store at USP controlled room temperature 20° C to 25° C (68° F to 77° F); excursions permitted between 15° C to 30° C (59° F to 86° F)

Preparation & Administration

MABS PREPARATION & ADMINISTRATION

Upon receipt of mAbs product(s), providers must adhere to the following federal requirements:

1) Administration preparation process:

- Prepare sterile infusions in a manner consistent with local laws, regulations, guidelines and policies
- Obtain new vial(s) and/or IV bags if the drug product contains any visible particulate matter

2) Needs for space to prepare mAb drug:

- Dedicated preparation area, in addition to sufficient administration capacity onsite or nearby

3) Acceptable equipment for mAb drug storage:

- Refrigerated storage (2-8° C)
- Temperature control mechanism, including temperature monitoring process

mAbs can be prepared for infusion and subcutaneous administration bedside by any qualified medical professional.

Please see EUA manufacturer fact sheet for drug-specific requirements.

ORAL ANTIVIRALS PREPARATION & ADMINISTRATION

Upon receipt of oral antiviral product(s), providers must adhere to the following requirements:

1) Dosage & administration:

- **Molnupiravir:** The dosage in adult patients is 800 mg (four 200 mg capsules) taken orally every 12 hours for five (5) days, with or without food
  - Take molnupiravir as soon as possible after a diagnosis of COVID-19 has been made, and within five (5) days of symptom onset
  - Completion of the full five-day treatment course and continued isolation in accordance with public health recommendations are important to maximize viral clearance and minimize transmission of SARS-CoV-2
  - Molnupiravir is not authorized for use for longer than five (5) consecutive days because the safety and efficacy have not been established
- **PAXLOVID (Standard Dosage):** The dosage for PAXLOVID is 300 mg nirmatrelvir (two 150 mg tablets) with 100 mg ritonavir (one 100 mg tablet) with all three tablets taken together orally twice daily for five (5) days, with or without food
  - Prescriptions should specify the numeric dose of each active ingredient within PAXLOVID
  - Completion of the full five-day treatment course and continued isolation in accordance with public health recommendations are important to maximize viral clearance and minimize transmission of SARS-CoV-2
- **PAXLOVID (Renal Dosage):** The dosage for PAXLOVID is 150 mg nirmatrelvir (one 150 mg tablet) with 100 mg ritonavir (one 100 mg tablet) with all two tablets taken together orally twice daily for five (5) days, with or without food
  - Dosage required for patients with moderate renal impairment (eGFR ≥30 to <60 mL/min). No dosage adjustment is needed in patients with mild renal impairment (eGFR ≥60 to <90 mL/min). PAXLOVID is not recommended in patients with severe renal impairment (eGFR <30 mL/min). Please refer to the HCP Letter for further information
  - Prescriptions should specify the numeric dose of each active ingredient within PAXLOVID
  - Completion of the full five-day treatment course and continued isolation in accordance with public health recommendations are important to maximize viral clearance and minimize transmission of SARS-CoV-2

2) Acceptable equipment for oral antiviral drug storage:

- USP Controlled Room Temperature 20° C to 25° C (68° F to 77° F)
- Excursions permitted between 15° C to 30° C (59° F to 86° F)

Please see EUA manufacturer fact sheet for drug-specific requirements.

VACCINATION CONSIDERATIONS

Following updated guidance from the CDC, it is **no longer necessary to delay COVID-19 vaccination following receipt of monoclonal antibodies**.

People who received passive antibody products

- People who previously received antibody products (anti-SARS-CoV-2 monoclonal antibodies or convalescent plasma) as part of COVID-19 treatment, post-exposure prophylaxis, or pre-exposure prophylaxis can be vaccinated at any time; **COVID-19 vaccination does not need to be delayed following receipt of monoclonal antibodies or convalescent plasma**. Although some reduction in vaccine-induced antibody was observed in people who previously received antibody products, the clinical significance of this reduction is unknown, and the balance of benefits vs. risks favors proceeding with vaccination even considering the possibility of diminished vaccine effectiveness in this situation.
- **However, in people who previously received a COVID-19 vaccine, administration of tixagevimab/cilgavimab (EVUSHELD) for pre-exposure prophylaxis should be deferred for at least two weeks after vaccination**, per the product EUA.

Additional considerations

- Providers should consult treatment guidelines for use of monoclonal antibodies as pre-exposure prophylaxis for moderately or severely immunocompromised people who may not mount an immune response to COVID-19 vaccination.

For more information, please see the CDC's interim vaccine guidelines.

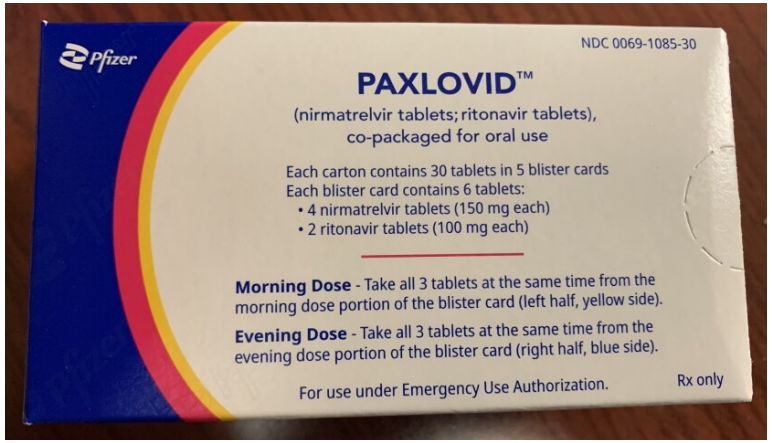
PAXLOVID PACKAGING & DOSAGE INFORMATION

Please be aware that PAXLOVID has multiple packaging types, and it is essential you take note of the differences when requesting and prescribing the product.

Packaging: The PAXLOVID™ may arrive in one of two (2) packaging configurations:

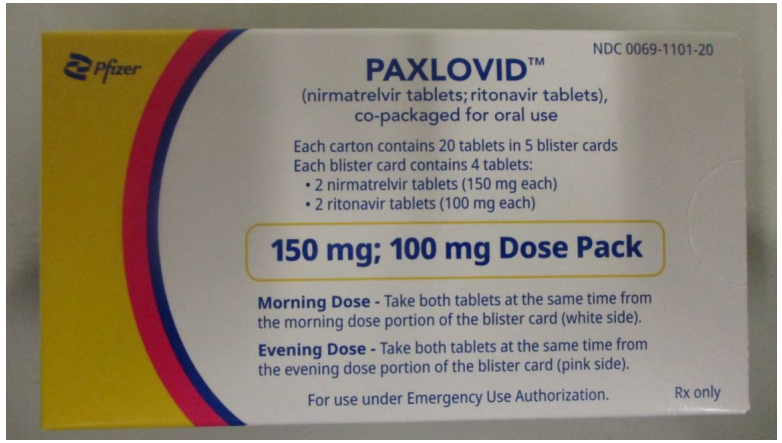
For patients without, or with mild, renal impairment (eGFR ≥60 mL/min):

PAXLOVID™ with 30 tablets - 300 mg nirmatrelvir (two 150 mg tablets) with 100 mg ritonavir (one 100 mg tablet)



For patients with moderate renal impairment (eGFR ≥30 or <60 mL/min):

PAXLOVID™ with 20 tablets - 150 mg nirmatrelvir (one 150 mg tablets) with 100 mg ritonavir (one 100 mg tablet)



It is important that providers and those requesting and/or prescribing the product pay close attention to the dosage and refer to the QR code enclosed with the product for updates. Please refer to the HCP Letter for the latest information and instructions for each dosage.

Post-Treatment Monitoring

POST-TREATMENT PATIENT MONITORING

mAbs

1. Providers should clinically monitor patients for at least **one hour** after infusion is complete for reactions
2. Provide to and review with the patient: COVID-19 Antibody Therapy Discharge Instructions
3. Patients treated with monoclonal antibody therapy should continue to use infection precautions and isolate or quarantine according to CDC Criteria for Quarantine and Isolation
4. Administrators of monoclonal antibody therapy should report all medication errors and serious adverse events within seven (7) days from the onset of the event. This can be found here: http://www.fda.gov/medwatch/report.htm. Please note, all fields should be completed with as much detailed information as possible

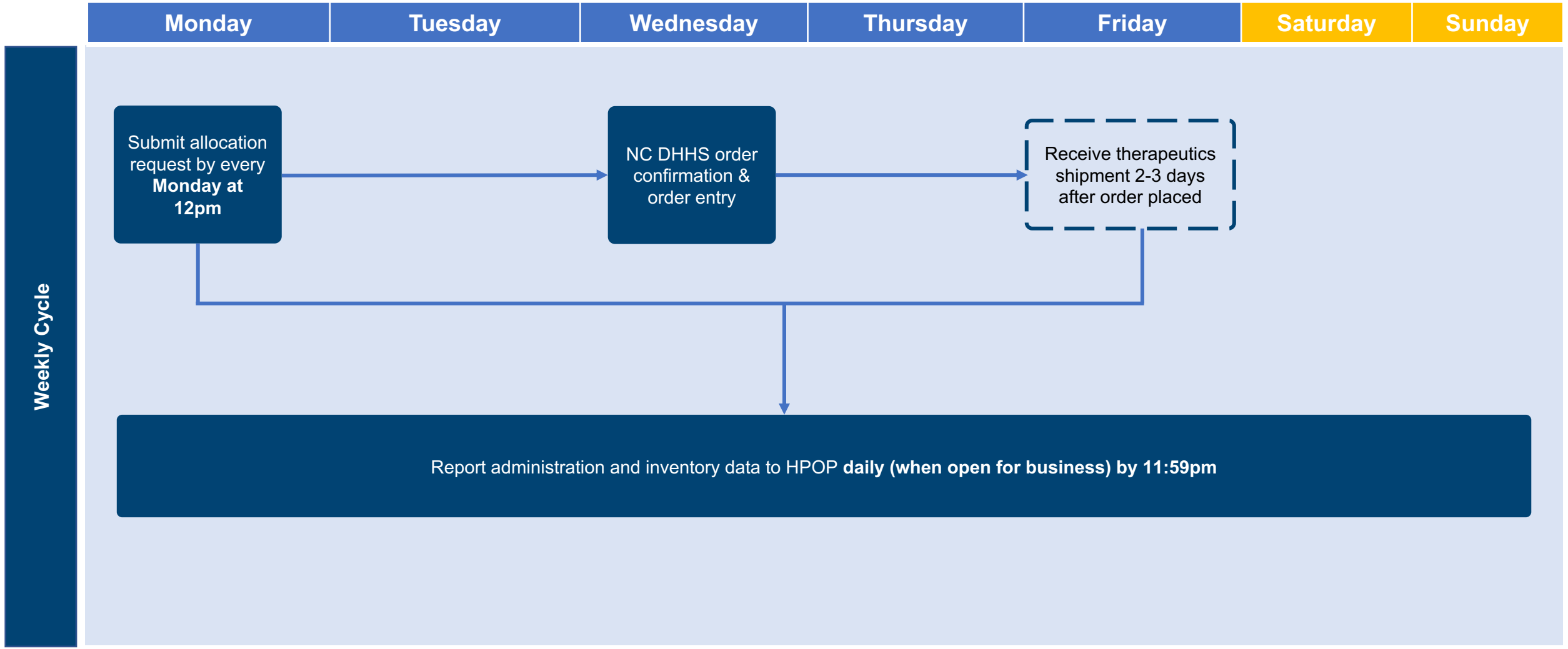
Oral Antivirals

1. No drug interactions have been identified based on the limited available data on the emergency use of molnupiravir authorized under this EUA
2. Refer to Pfizer's Potentially Significant Drug Interactions, or the EUA Fact Sheet for PAXLOVID to identify potential drug interactions with PAXLOVID
3. Treatment of overdosage for molnupiravir and PAXLOVID should consist of general supportive measures, including monitoring of vital signs and observations of the clinical status of the patient

Reporting & Billing

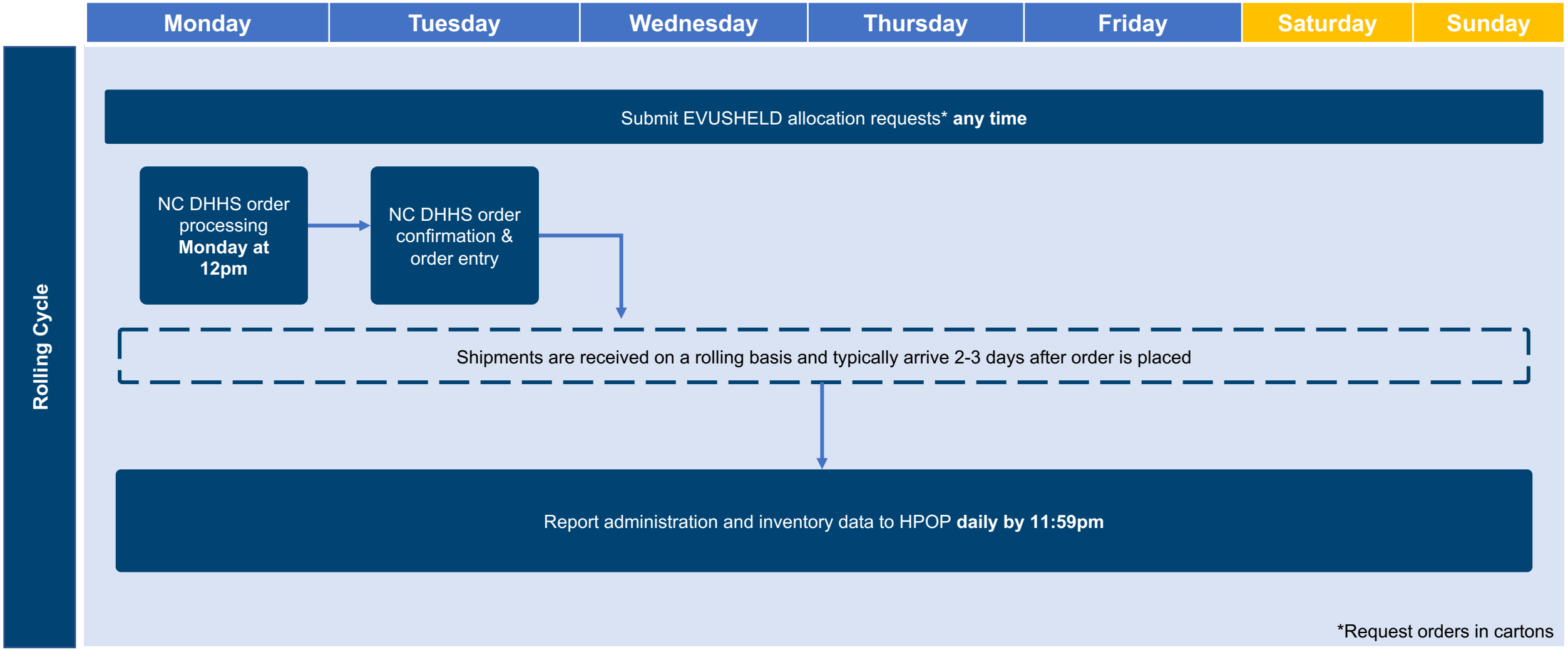
PROVIDER THERAPEUTICS ALLOCATION REPORTING CADENCE

The graphic below illustrates provider cadence for oral antivirals and bebtelovimab allocation requests and reporting to NC DHHS and HHS.



PROVIDER EVUSHELD ALLOCATION REPORTING CADENCE

The graphic below illustrates new provider cadence for EVUSHELD allocation requests and reporting to NC DHHS and HHS.



REPORTING REQUIREMENTS

Providers should report currently authorized therapeutics (EVUSHELD, molnupiravir, PAXLOVID, and bebtelovimab) in HPOP, and report previously authorized therapeutics (sotrovimab, REGEN-COV, and Bam/Ete) to NC DHHS and HHS Tele-tracking. See below for additional guidance:

For Currently Authorized COVID-19 Therapeutics:

Although the NC DHHS oversees distribution and management of EVUSHELD, Oral Antivirals (molnupiravir and PAXLOVID), and bebtelovimab to provider locations within the state, **ALL administrating locations must report administration and inventory data in HPOP DAILY for all days the location is open**. Reporting is not required when the facility is closed and not available for administering or dispensing. Daily reporting must include what you have administered since you last reported and is **NOT** cumulative. EVUSHELD should be reported in cartons, all other therapeutics should be reported in courses.

Please reference this document for the correct way to report administrations and inventory in HPOP.

For Previously Authorized COVID-19 Therapeutics:

The Federal government continues to encourage providers to hold on to previously authorized therapeutics, including sotrovimab, REGEN-COV, and bamlanivimab/etesevimab. Providers should continue to report weekly inventory levels of these products via the following mechanisms:

1. Federal HHS Utilization Report via HHS Tele-Tracking due Wednesdays at 11:59pm (not applicable for hospitals)
2. North Carolina Weekly COVID-19 Therapeutic Inventory Form due Wednesdays at 12:00pm (applicable to all providers)

Weekly reminders and instructions will also continue to be emailed to existing providers from TeleTracking's Technical Support at hhs-protect@teletracking.com.

First-time users will receive enrollment and reporting instructions in an e-mail from protect-noreply@hhs.gov with the subject line of "Invitation: HHS TeleTracking COVID-19 Portal." This email provides step-by-step instructions to access the Portal for the first time.

ADVERSE EVENT REPORTING

The prescribing healthcare provider and/or the provider's designee are/is responsible for mandatory reporting of all serious adverse events and medication errors potentially related to the respective drug product within seven (7) days from the healthcare provider's awareness of the event, using FDA Form 3500 (for information on how to access this form, see below).

Submit adverse event and medication error reports, using Form 3500, to FDA MedWatch using one of the following methods:

- Complete and submit the report online by visiting www.fda.gov/medwatch/report.htm
- Complete and submit a postage-paid FDA Form 3500 and return by:
  - Mail to MedWatch, 5600 Fishers Lane, Rockville, MD 20851-9787, or
  - Fax to 1-800-FDA-0178
- Call 1-800-FDA-1088 to request a reporting form

Please provide a copy of all FDA MedWatch forms to:

Product	Company	E-mail/Website	Fax Number	Phone Number
REGEN-COV	Regeneron Pharmaceuticals	medical.information@regeneron.com	1-888-876-2736	1-844-734-6643
Bam/Ete	Eli Lilly and Company	mailindata_gsmtindy@lilly.com	1-317-277-0853	1-855-545-5921
Sotrovimab	GlaxoSmithKline	WW.GSKAEReportingUS@gsk.com	1-919-287-2902	1-866-475-2684
EVUSHELD	AstraZeneca	https://contactazmedical.astrazeneca.com	1-866-742-7984	1-800-236-9933
PAXLOVID	Pfizer	www.pfizersafetyreporting.com	1-866-635-8337	1-800-438-1985
Molnupiravir	Merck Sharp & Dohme Corp.	dpoc.usa@msd.com	1-215-616-5677	
VEKLURY	Gilead Sciences, Inc.	safety_fc@gilead.com	1-650-522-5477	1-800-445-3235
Bebtelovimab	Eli Lilly and Company	mailindata_gsmtindy@lilly.com	1-317-277-0853	1-855-545-5921

BILLING & REIMBURSEMENT

Please reference the following link for more detailed billing information:

- COVID-19 Monoclonal Antibody: Coding and Billing Guide
- Centers for Medicare & Medicaid Services (CMS) Guidance on Oral Antiviral Billing
- National Community Pharmacists Association COVID-19 Antivirals Dispensing and Reimbursement

CMS Code for Outpatient use of VEKLURY (remdesivir)

- Following the recent statement from National Institutes of Health (NIH) COVID-19 Treatment Guidelines Panel regarding therapies for COVID-19 Omicron variant, CMS created **HCPCS code J0248** for the VEKLURY (remdesivir) antiviral medication when administered in outpatient setting
- Code available for use by all payers
- Effective dates of service on or after December 23, 2021:
  - Long descriptor: Injection, remdesivir, 1 mg
  - Short descriptor: Inj, remdesivir, 1 mg
- Medicare Administrative Contractors (MACs) determine Medicare coverage when no national coverage determination, including when providers use FDA-approved drugs for indications other than what is on approved label
- MACs will determine Medicare coverage for HCPCS code J0248 for VEKLURY (remdesivir) administered in outpatient setting
- See CMS COVID-19 Provider Toolkit for additional information

Comms

THERAPEUTICS COMMUNICATION

Providers can subscribe to the **NC DHHS Therapeutics Communication** to learn more about weekly updates and news. Weekly updates are sent out on Wednesdays. Confirmation of allocation request receipt is sent out on Fridays.

To get added to the distribution list, complete the NC DHHS Therapeutics Provider Communications form:

- If you would like to **add more than one email** to the distribution list, refresh page after submission and resubmit
- **Please note**, that there will be a separate link shared for new providers to register for a mAbs or oral antivirals account. Completing this form will only get you added to the NC DHHS therapeutics communications distribution list

Additional Resources

ADDITIONAL RESOURCES

Therapeutics FAQs

Reference this site for FAQs regarding COVID-19 mAbs, oral antivirals, treatment, and other questions

NC Provider Office Hours

Attend bi-weekly Teams meetings on Fridays at 12pm for questions regarding therapeutic products and the ordering and allocation process (meeting invite link provided in Therapeutics Newsletter)

Therapeutics Inbox

Email the NC DHHS COVID-19 Therapeutics Inbox (Therapeutics.COVID19@dhhs.nc.gov) for urgent issues

Deauthorized Products

Please refer to this section for guidance on deauthorized products: REGEN-COV and Bam/Ete are not authorized for use at this time due to their markedly reduced activity against the Omicron variant, Sotrovimab is not authorized for use at this due to its markedly reduced activity against the BA.2 Omicron sub-variant.

Deauthorized Products

PRODUCT SPECIFICATIONS - DEAUTHORIZED

REGEN-COV

Please note: treatment is not authorized for use at this time due to the markedly reduced activity against the Omicron variant

- Manufactured by: Regeneron
- Authorized dosage for REGEN-COV for both treatment and as post-exposure prophylaxis is 600 mg of casirivimab and 600 mg of imdevimab administered together
- REGEN-COV is authorized for patients aged 12 and over
- For treatment, IV infusion is recommended
- Subcutaneous injection (shots administered underneath the skin) is an alternative route of administration when IV infusion is not feasible and would lead to delay in treatment
- For post-exposure prophylaxis, either intravenous infusion or subcutaneous injection is appropriate
- Providers should clinically monitor patients for at least one hour following the infusion/ injection for reactions
- Mixing and Dosing Instructions (linked)
- Visit the Health Care Provider Fact Sheet for further provider guidance and information

Bamlanivimab/Etesevimab

Please note: treatment is not authorized for use at this time due to the markedly reduced activity against the Omicron variant

- Manufactured by: Eli Lilly
- Authorized dosage for Bam/Ete for treatment is 700 mg of bamlanivimab and 1400 mg of etesevimab administered together
- Treatment can only be administered through an IV infusion of bamlanivimab and etesevimab as a single intravenous infusion via pump or gravity
- For post-exposure prophylaxis, use the same dosage as treatment and administer through IV infusion
- Authorized for post-exposure prophylaxis and treatment in all younger pediatric patients, including newborns
- The IV infusion will take 21-60+ minutes, dependent upon the providers' discretion
- Providers should clinically monitor patients for at least one hour after infusion is complete for reactions
- Mixing and Dosing Instructions (linked)
- Visit the Health Care Provider Fact Sheet for further provider guidance and information

Sotrovimab

Please note: treatment is not authorized for use at this time due to the markedly reduced activity against BA.2 Omicron sub-variant

- Manufactured by: GlaxoSmithKline
- Authorized dosage for sotrovimab for treatment is 500 mg of sotrovimab
- Sotrovimab is authorized for patients aged 12 and over
- Treatment can only be administered through IV infusion
- The IV infusion should administer the entire bag of solution over 30 minutes when using a 100mL infusion bag, or should be adjusted to 15 minutes when using a 50mL infusion bag
- Providers should clinically monitor patients for at least one hour after infusion is complete for reactions
- Mixing and Dosing Instructions (linked)
- Visit the Health Care Provider Fact Sheet for further provider guidance and information

DEAUTHORIZED MONOCLONAL ANTIBODIES – OVERVIEW

Please note: REGEN-COV and Bam/Ete are not authorized for use at this time due to their markedly reduced activity against the Omicron variant, Sotrovimab is not authorized for use at this due to its markedly reduced activity against the BA.2 Omicron sub-variant

Monoclonal antibodies, or mAbs, are antibodies made in a laboratory to fight a particular infection. The Food and Drug Administration (FDA) has issued **Emergency Use Authorization (EUA)** for the use of monoclonal antibody therapies for adult and pediatric patients aged 12 and older (Bam/Ete authorized for all ages). mAbs are given to patients with an infusion, subcutaneous injection, or intramuscular injection. They are used for treatment or prevention. As previously mentioned, the following are not authorized for use for COVID-19 at this time:

Generic Name	Also known as	Authorized Indication	Route of Administration	Dosing Regimen	Authorized Patient Population	Standing Order?*	Efficacy
Casirivimab / imdevimab	**REGEN-COV**	Post-exposure Prophylaxis, Treatment within 10 days of symptoms	Subcutaneous Injection; Intravenous Infusion	600 mg of both	Patients aged 12 years and older	No, rescinded January 24th	70% effective in preventing hospitalizations or deaths within five (5) days of symptom onset Reduced efficacy against Omicron
Bamlanivimab / etesevimab	**Bam/Ete**	Post-exposure Prophylaxis, Treatment within 10 days of symptoms	Intravenous Infusion	Dosage varies with weight	Patients of all ages, including neonates	No, rescinded January 24th	87% effective in preventing hospitalizations or deaths within five (5) days of symptom onset Reduced efficacy against Omicron
Sotrovimab	**Sotrovimab**	COVID-19 Treatment **within seven (7) days** of symptoms	Intravenous Infusion	500 mg of sotrovimab	Patients aged **12 years and older** and weighing at least 40 kg	No, rescinded April 6th	**79% effective** in preventing hospitalizations or death. Limited effectiveness against the BA.2 Omicron sub-variant

**Per the Public Readiness and Emergency Preparedness Act, pharmacies were added to the eligible providers and can now administer monoclonal antibody treatment*

REGEN-COV PACKAGING & LABELING INFORMATION

Please be aware that REGEN-COV has multiple packaging types. While REGEN-COV is no longer authorized for administration as COVID-19 treatment, providers should remain familiar with package types and labeling described below.

Packaging: The REGEN-COV™ may arrive in one of two (2) packaging configurations:

1) REGEN-COV™ Dose Packs (2-Vial) or
2) Casirivimab and Imdevimab Co-Pack (two (2) vials per carton): **One Carton allows for preparation of two (2) treatment doses**

It is important that providers and those mixing and/ or administering the product pay close attention to the dosage and refer to the QR code enclosed with the product for updates. Please refer to the Labeling and Packaging one pager and Regeneron website for the latest information and instructions for each formulation.

Labeling:

- In addition to the packaging configurations noted above, some REGEN-COV™ carton and vial labels may have statements such as “Solution for Intravenous Administration” or “For Intravenous Infusion after Dilution.”
- Any of these REGEN-COV™ vials may be used to prepare and administer intravenous infusions as well as subcutaneous injections, even though there is no language on the label that that states the subcutaneous route is appropriate.

Please send all questions to: Therapeutics.COVID19@dhhs.nc.gov